REMARKS

The Office Action of December 2, 2005 presents the examination of claims 1, 4-10, 16-23, 28 and 29. The present paper amends claims 1 and 16. Claims 6 and 7 are deemed allowed.

Amendments to the claims

Claim 1 is amended to correct minor editorial errors. Specifically, the "renumbering" of the alternatives in claim 1 by the prior amendment was not carried through into the description of the alternatives themselves. This has been corrected. Claim 16 is amended to adopt the suggestions of the Examiner to use a definite article in a dependent claim and to utilize a more common expression for the relation of the coding sequence to the promoter. Neither amendment affects the scope of the claims.

Rejections under 35 U.S.C. § 112, first paragraph

Written Description

Claims 1, 4, 5, 8-10, 16-23, 28 and 29 stand rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of written description support. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

The rejection is maintained as previously stated by the Examiner. That is, the Examiner alleges that Applicants do not provide sufficient disclosure to demonstrate that they were in possession of the invention of scope broader than the specific amino acid sequence of SEQ ID NO: 5 at the time the application was filed. The Examiner takes a position that, among three particular protein sequences specifically disclosed, the Applicant has demonstrated actual raffinose synthase activity for only SEQ ID NO: 5, and (as part of an enablement rejection) that an assertion of biological activity based upon amino acid sequence homology is insufficient.

First, as a legal matter, absent sound scientific reasoning or evidence to the contrary, the Examiner must accept as true allegations made in the specification. *See, e.g. In re Marzocchi*, 169 USPQ 137 (CCPA 1971).

In the present instance, the specification describes the complete amino acid sequence of at least two raffinose synthase proteins (SEQ ID NO: 3 and SEQ ID NO: 5). The specification also discloses a partial amino acid sequence of two additional raffinose synthase proteins (SEQ ID NO: 1 and SEQ ID NO: 7). The specification describes how to obtain a raffinose synthase cDNA using the polymerase chain reaction amplification method using particular primers described by sequence, and discloses plant sources with which those primers may be used. The specification further describes how to express the cDNA in both bacterial and plant hosts. The specification provides an assay for raffinose synthase biological activity. The specification states, based upon the high degree of amino acid sequence homology (i.e. about 70% identity or higher), it is expected that the protein of SEQ ID NO: 3 will exhibit raffinose synthase activity. There are working examples that show actual reduction to practice of two complete cDNAs (SEQ ID NOs: 3 and 5) encoding raffinose synthase proteins and two partial cDNAs encoding the major part of additional raffinose synthase proteins; these clones are obtained from diverse genera using the materials and methods generally described in the specification. The specification also teaches a method for obtaining the complete cloned cDNA, and hence corresponding amino acid sequence and means for expressing it, for the raffinose synthase cDNA encoding SEQ ID NOs: 1 and 7.

There is evidence in the record, in the form of Dr. Watanabe's Declaration, that the protein of amino acid sequence SEQ ID NO: 5 has activity of a raffinose synthase.

None of these facts are disputed by the Examiner. It is most difficult to understand then, how a conclusion that Applicants did not broadly "possess" the claimed invention at the time of filing can be reasonably alleged.

The Examiner asserts that Applicants have only demonstrated actual raffinose synthase activity for the protein of SEQ ID NO: 5.

Applicants would also point the Examiner to disclosure in the companion application no. 08/992,914, which shows that the cDNA obtained from broad bean (*V. faba*, SEQ ID NO: 1 of the '914 application) also encodes an a protein having raffinose synthase activity. (*See* Table 1 of that specification.) The *V. faba* sequence has about 62% amino acid sequence identity to SEQ ID NO: 5 (from mustard) of the present application (*see* Table 2 of the Watanabe Declaration II attached). Thus, the present record now contains evidence that demonstrates unequivocally that Applicants' assertion in the present specification that a protein having at least 70% identity to SEQ ID NO: 3 (or 5 or 7) has raffinose synthase activity is correct.

The Examiner is reminded that Applicants' burden is only to show by the preponderance of the evidence that the specification establishes "possession" of the invention of broad scope. Applicants submit that the record at present is sufficient to meet this burden. Absent strong evidence in rebuttal of the showings of the Watanabe Declaration, and the disclosure of the '914 application, that two of two proteins identified as putative raffinose synthases according to the teachings of the present specification do indeed have that activity, the Examiner must withdraw the present rejection.

The Examiner is apparently requiring that Applicants limit the scope of their claims only to the working examples, but such is not the requirement of the patent laws. In fact, the written description requirement can be adequately met in the complete absence of any working example or any demonstration of actual reduction to practice. *See, e.g. Falkner v. Inglis*, ___, Case no. 05-1324 (Fed. Cir. 2006), copy attached.

Applicants submit that the present application very well demonstrates "possession" of the invention, throughout the full scope as presently claimed. As explained above, the specification discloses actual reduction to practice of two full-length cDNA clones, one of which has been actually demonstrated to encode raffinose synthase activity, and two partial cDNA clones, which

were obtained from diverse genera of plants, including specific examples for beet and mustard and rapeseed. The specification also describes a set of PCR primers that can be used to obtain clones from enumerated genera of plants. There is a test for actual raffinose synthase activity described in the specification so that clones so obtained can be confirmed in their activity. There is evidence of record that one of ordinary skill in the art can distinguish a raffinose synthase protein from the stachyose synthase and seed imbibation proteins of different utility based upon sequence homology to the reference sequences in the specification in the manner set forth in the specification. Accordingly, the instant rejection of claims 1, 4, 5, 8-10, 16-23, 28 and 29 under 35 U.S.C. § 112, first paragraph, for alleged lack of written description support, should be withdrawn.

Enablement

Claims 1, 4, 5, 8-10, 16-23, 28 and 29 remain rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement by the specification. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

Again, the Examiner's position is that Applicants have only demonstrated actual raffinose synthase activity for one protein. The Examiner then argues that merely because the degree of sequence identity to SEQ ID NO: 3 (or 5 or 7) of the amino acid sequence of an "unknown" protein is as high as 70%, that protein would not necessarily exhibit raffinose synthase activity and in fact is just as likely to exhibit stachyose synthase activity or seed imbibation protein activity. The Examiner alleges that the stachyose synthases as a family have a degree of sequence identity that falls within the degree of identity set forth in the present application.

This is not persuasive of lack of enablement. The Examiner is reminded that it is his burden to establish a *prima facie* lack of enablement, i.e. to establish that undue experimentation is required for one of ordinary skill in the art to practice the present invention throughout its claim scope. The amount of experimentation needed is not determinative; rather the question is

whether the necessary experimentation is "undue". *In re Wands,* 8 USPQ2d 1400 (Fed. Cir. 1988).

The Examiner must consider not only the breadth of the claims, but also the nature of the invention, the amount of experimentation needed the level of ordinary skill in the art, the guidance provided by the specification and by the state of the prior art, and the predictability of the art. All of these factors must be considered. *Wands, ibid.*

The Examiner's position is essentially that it is unpredictable, based upon sequence homology alone, whether a given protein would actually be a raffinose synthase as opposed to being a stachyose synthase or a seed imbibation protein. Applicants submit that the Examiner has not properly considered all of the factors that need to be weighed and so has incorrectly determined that the specification does not enable the presently claimed invention.

As a threshold matter, there is evidence of record in the application, though not previously provided in Declaration form, in Table 1, Table 2 and Figure 1 filed with Applicants' paper of February 11, 2004, that demonstrates that the degree of sequence identity among raffinose synthases is at least 50%, the degree of sequence identity among stachyose synthases is at least 64%, and the degree of sequence identity between a raffinose synthase and a stachyose synthase or seed imbibation protein is only as high as 44%. Thus, one of ordinary skill in the art, merely comparing an amino acid sequence of a protein to SEQ ID NO: 3 (or 5 or 7) can easily preliminarily determine whether or not it is a raffinose synthase (% identity > 50%) or a stachyose synthase (% identity <44%) or a seed imbibation protein (% identity < 39%). The Examiner's basic premise is therefore incorrect.

So that the Examiner can perhaps give a bit more weight to this evidence, Applicants provide attached hereto a Declaration of Dr. Watanabe ("Watanabe Declaration II") filed in the companion application no. 08/992,914, which provides similar data, together with detailed explanation of the analysis and a statement of conclusion similar to the above conclusion.

Once a protein is identified as a putative raffinose synthase, the artisan can then perform the expression and assay tests described in the specification to confirm this preliminary determination. Experimentation that is set forth in the specification as useful for confirming hypotheses regarding activity of an enzyme must be considered to be guided and expected, not "undue".

The breadth of the claims encompasses raffinose synthases obtained by amplification of nucleic acids obtained from "beet", "mustard" and "rapeseed". The specification discloses specific primer sequences that can be used in such amplification procedures, and furthermore includes working examples that demonstrate isolation of cDNAs encoding raffinose synthases from an example of each of these genera of plants. There is Declaration evidence of record (the Watanabe Declaration) showing that one of the clones isolated has activity as a raffinose synthase by the assay method disclosed in the specification when expressed in a plant. (*See*, page 31, lines 24-25 of the specification.)

The level of ordinary skill in the art of isolating genes from plants and characterizing the encoded proteins is generally accepted to be high. Therefore, the experimentation described in the specification as needed to obtain clones from diverse plants, compare their sequences to one of SEQ ID NO: 3, 5 or 7 to identify putative raffinose synthases, express the encoded proteins and then perform the activity assay as described in the specification is well within the skill of the ordinary artisan.

The Examiner seems to believe that, because the stachyose synthases were not described at the level of a molecular clone of encoding DNA at the time the present invention was made, Applicants could not have discriminated between raffinose synthases and stachyose synthases by mere sequence homology. Applicants are not certain why the later discovery of the actual sequence of a stachyose synthase protein is at all relevant. Applicants note that the specification teaches that sequence homology provides a hypothesis that a protein is a raffinose synthase and that the specification teaches a biochemical assay for raffinose synthase activity that one of ordinary skill in the art may apply to confirm that hypothesis. The lack of ability of one of

ordinary skill in the art to develop an alternative hypothesis that a protein might be a stachyose synthase by comparison to a reference stachyose synthase protein sequence is irrelevant to enablement of the present invention.

As to the particular references cited by the Examiner, Applicants note that, if anything, they improve the ability of a skilled artisan to distinguish a raffinose synthase from a stachyose synthase. In particular, Applicants note that *Peterbauer et al. 2002* at page 841, right column, point out "a block of about 80 amino acids, which is exclusively present in stachyose synthases."

This "block of about 80 amino acids" that is not contained in the amino acid sequence of raffinose synthase is plainly shown in *Peterbauer et al. 1999*, in Fig. 2. Note the peptide sequence from amino acid 213-287 shown in VaSTS1 and absent from all RFS proteins shown. Thus, a gene enoding an amino acid sequence containing such "a block of about 80 amino acids" which is not contained in the amino acid sequence of raffinose synthase can be discarded as a gene having a structural characteristic which is not contained in raffinose synthase gene by comparing its amino acid sequence to the amino acid sequences represented by SEQ ID NOS: 3 and 5 of the present application.

While such further criterion may strengthen the hypothesis held by one of skill in the art practicing the invention, it's unavailability at the time the present application was filed does not establish that the present specification does not enable the presently claimed invention.

For all of the above reasons, Applicants submit that the experimentation required to practice the present invention throughout its scope is not undue. Accordingly, the instant rejection of claims 1, 4, 5, 8-10, 16-23, 28 and 29 under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement by the specification, should be withdrawn.

Applicants believe the pending application is in condition for allowance and such favorable action on the merits is respectfully requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Mark J. Nuell (Reg. No. 36,623) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

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Respectfully submitted,

By _____

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Attachment: Declaration Under 37 C.F.R. § 1.132, Watanabe
Falkner v. Inglis, CAFC, 05-1324, Interference No. 105,187